

IN THE CLAIMS

Claims 1-20 are pending. Claims 1-19 stand rejected and claim 20 has been restricted by the Examiner. Please cancel claims 8 and 18 without prejudice. Please amend claims 1-7, 9-17 and 19 to read as follows. Please add new claims 21-37. A marked-up version of the claims showing deletions and insertions is provided in the appendix to this paper.

1. (Twice Amended) A method of regulating adenovirus packaging comprising the steps of:

(a) obtaining a helper adenovirus vector containing a first adenovirus packaging sequence comprising a repressor binding site;

(b) obtaining a DNA delivery adenovirus vector comprising 5' and 3' inverted terminal repeats; a second adenovirus packaging sequence; a heterologous gene; and a promoter operatively linked to the heterologous gene;

(c) propagating the helper adenovirus vector and the DNA delivery adenovirus vector in a cell-line; and

(d) repressing packaging of the helper adenovirus vector by a repressor which binds to the repressor binding site contained in the helper adenovirus vector.

2. (Twice Amended) The method according to claim 1 wherein the repressor is COUP-TF.

3. (Twice Amended) The method according to claim 1 wherein the repressor is *lac* repressor.

4. (Twice Amended) The method according to claim 1 wherein the propagating step occurs in a first cell-line and the repressing step occurs in a second cell-line, wherein the repressing step in the second cell-line further comprises a step selected from the group of steps consisting of:

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- (a) endogenously expressing the repressor; and
  - (b) transfecting a vector expressing the repressor.

5. (Twice Amended) The method according to claim 1 wherein the repressing step occurs in the cell-line of step (c) and wherein the repressing step further comprises a step selected from the group of steps consisting of:

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- (a) endogenously expressing the repressor; and
  - (b) transfecting a vector expressing the repressor.

6. (Twice Amended) A helper adenovirus vector comprising an adenovirus packaging sequence containing a plurality of COUP-TF binding sites comprising an A repeat VI element.

7. (Twice Amended) A helper adenovirus vector comprising an adenovirus packaging sequence having at least two copies of 5'-TTTGN<sub>8</sub>CG-3'(SEQ ID NO:1) and a plurality of COUP-TF binding sites, comprising an A repeat VI element.

9. (Twice Amended) A method of administering a replicant defective adenovirus to a mammal comprising the steps of:

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3  
1
- (a) packaging a DNA delivery adenovirus vector according to the method of claim 1;
  - (b) isolating the packaged DNA delivery adenovirus vector;
  - (c) preparing the packaged DNA delivery adenovirus vector in a pharmaceutically acceptable carrier; and
  - (d) administering the prepared and packaged DNA delivery adenovirus vector to said mammal.

10. (Twice Amended) A helper adenovirus vector comprising a packaging signal sequence consisting of at least two copies of 5'-TTTGN<sub>8</sub>CG-3'(SEQ ID NO:1) and an A repeat VI element.

11. (Twice Amended) The helper adenovirus vector according to claim 10 wherein a repressor binding site is embedded in the packaging signal sequence.

12. (Twice Amended) The helper adenovirus vector according to claim 10 wherein a repressor binding site flanks the packaging signal sequence.

13. (Twice Amended) The helper adenovirus vector according to claim 10 wherein a repressor binding site alternates with the packaging signal sequence.

14. (Once Amended) The helper adenovirus vector according to claim 10 having 3-12 copies of the packaging signal sequence.

15. (Twice Amended) The helper adenovirus vector according to claim 14 wherein a repressor binding site is located between packaging signal sequences.

16. (Twice Amended) The helper adenovirus vector according to claim 11 or 15 wherein the repressor binding site is a *lac* repressor binding site.

17. (Twice Amended) The helper adenovirus vector according to claim 11 or 15 wherein the repressor binding site is a E2F binding site.

19. (Twice Amended) The method of administering a replicant defective adenovirus to a mammal according to claim 9, wherein step (a) is conducted with a helper adenovirus according to claims 6, 7 or 10.

Please add the following new claims, i.e., claims 21-37:

21. (New) A method of regulating adenovirus packaging comprising the steps of:

(a) obtaining a helper adenovirus vector containing a first adenovirus packaging sequence;

(b) obtaining a DNA delivery adenovirus vector comprising 5' and 3' inverted terminal repeats; a second adenovirus packaging sequence comprising a repressor binding site; and a promoter operatively linked to the heterologous gene;

(c) propagating the helper adenovirus vector and the DNA delivery adenovirus vector in a cell-line; and

(d) repressing packaging of the DNA delivery adenovirus vector by a repressor which binds to the repressor binding site contained in the DNA delivery adenovirus vector.

22. (New) The method according to claim 21 wherein the repressor is COUP-TF.

23. (New) The method according to claim 21 wherein the repressor is *lac* repressor.

24. (New) The method according to claim 21 wherein the propagating step occurs in a first cell-line and the repressing step occurs in a second cell-line, wherein the repressing step further comprises a step selected from the group of steps consisting of:

- (a) endogenously expressing the repressor; and
- (b) transfecting a vector expressing the repressor.

25. (New) The method according to claim 21 wherein the repressing step occurs in the cell-line of step (c) and wherein the repressing step further comprises a step selected from the group of steps consisting of:

- (a) endogenously expressing the repressor; and
- (b) transfecting a vector expressing the repressor.

26. (New) A DNA delivery adenovirus vector comprising an adenovirus packaging sequence containing a plurality of COUP-TF binding sites comprising an A repeat VI element.

27. (New) A DNA delivery adenovirus vector comprising an adenovirus packaging sequence having at least two copies of 5'-TTTGN<sub>8</sub>CG-3'(SEQ ID NO:1) and a plurality of COUP-TF binding sites, comprising an A repeat VI element.
28. (New) The DNA delivery adenovirus according to claim 26 or claim 27 further comprising a heterologous gene operatively linked to a promoter.
29. (New) A DNA delivery adenovirus vector comprising a packaging signal sequence consisting of at least two copies of 5'-TTTGN<sub>8</sub>CG-3'(SEQ ID NO:1) and an A repeat VI element.
30. (New) The DNA delivery adenovirus vector according to claim 29 wherein a repressor binding site is embedded in the packaging signal sequence.
31. (New) The DNA delivery adenovirus vector according to claim 29 wherein a repressor binding site flanks the packaging signal sequence.
32. (New) The DNA delivery adenovirus vector according to claim 29 wherein a repressor binding site alternates with the packaging signal sequence.
33. (New) The DNA delivery adenovirus vector according to claim 29 having 3-12 copies of the packaging signal sequence.
34. (New) The DNA delivery adenovirus vector according to claim 33 wherein a repressor binding site is located between packaging signal sequences.
35. (New) The DNA delivery adenovirus vector according to claim 30 or claim 34 wherein the repressor binding site is a *lac* repressor binding site.